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Good outcome of AIDS-related Burkitt lymphoma (BL) and diffuse large B-cell lymphoma (DLBCL) with abbreviated cycles of EPOCH-rituximab

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The addition of rituximab to CHOP chemotherapy may augment tumor response but in patients with low CD4 counts, one study suggested that this benefit may be offset by increased infectious deaths (Kaplan. *Blood* 2005; **106**:1538). We hypothesized that the addition of rituximab to EPOCH chemotherapy could improve tumor kill, allowing fewer cycles of treatment and therefore reducing toxicity.

Patients received EPOCH-R (in mg/m²/d – etoposide 50, vincristine 0.4 and doxorubicin 10 all CIV d 1–5; cyclophosphamide 750 mg IV d 5; prednisone 60 po days 1–5 and rituximab 375 IV d 1,5 and G-CSF sc d 6–15) every 21 days. Prophylactic IT methotrexate was administered and HAART was suspended during therapy. Cyclophosphamide was adjusted based on absolute neutrophil count (ANC) nadir. Response was assessed by CT and FDG-PET scan and patients received one cycle beyond CR for a minimum of three cycles. Characteristics of 40 enrolled patients are: median (range) age 42 (9–60) years; IPI 3 (0–4); ECOG PS 1 (1–4), CD4 count 222 (0–835) cells/mm³; HIV viral load 34,766 (0–6,080,000) RNA copies/mL; male sex 35 (88%); LDH > N 27 (68%); stage IV 27 (68%) and histology DLBCL 32 (80%) and BL 8 (20%). Of 38 evaluable patients (2NE), median (range) number of cycles given is three (3–5) with CR/CRu in 35 (92%) and PR in one (3%) patients.

All eight patients with Burkitt lymphoma are in continuous remission. At four years median potential follow-up, PFS and OS are 86 percent and 70 percent. For patients with CD4 > and < 100 cells/mm³ PFS is 96 percent and 69 percent, respectively. IPI did not impact OS and PFS. Early PET scanning (after cycle 2) had a very high negative predictive value (100%) but a low positive predictive value (20%). One treatment-related death occurred (from complications of mycobacterium avium intercellulare (MAI)) and other toxicity included fever or neutropenia on 30 percent, ANC < 500/mm³ on 40 percent, and platelets < 50,000 on 23 percent cycles. EPOCH-R was associated with less CD4 loss – median 128 cells/mm³ (range +154 to -639) compared to EPOCH alone (median 189 cells/mm³ (range +19 to -973). Abbreviated EPOCH-R is highly effective with acceptable tolerability in ARL and enables the administration of fewer treatment cycles (median 3 versus 6). Although patients with CD4 < 100/mm³ have good tumor control with EPOCH-R with a PFS of 70 percent at four years, overall survival for this group was only 31 percent due mainly to later deaths from complications of advanced AIDS. In contrast, patients with high CD4 counts > 100/mm³ have an extremely favorable outcome with and survival following EPOCH-R. The addition of rituximab did not appear to contribute to infection related complications or deaths. EPOCH-R showed excellent efficacy in eight patients with BL with an OS and PFS of 100 percent. PET scanning has a high negative but low positive

predictive value for subsequent relapse. Accrual continues.

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